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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,690	12/22/2000	Melis Anastasios	NREL 99-29	4270

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PAUL J WHITE, SENIOR COUNSEL
NATIONAL RENEWABLE ENERGY LABORATORY (NREL)
1617 COLE BOULEVARD
GOLDEN, CO 80401-3393

EXAMINER

AFREMOVA, VERA

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 08/08/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/748,690

Applicant(s)
Melis Anastasios

Examiner
Vera Afremova

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 19, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5-8, and 10 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-8, and 10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

Status of claims

Claims 1-3, 5-8 and 10 as amended are under examination in the instant office action [Paper No. 15 filed 5/15/2003].

Claims 4 and 9 were canceled by applicants [Paper No. 6 filed 5/28/2002].

Claim Objections

Claim 6 remains objected to because of the following informalities:

There are some typing errors in the claim. For example: article “a” as related to plural form of phrase “algae” in claim 6; coma before “and” in claim 6, line 2. Appropriate corrections are required.

Claim Rejections - 35 USC § 112

Claims 1-3, 5-8 and 10 as amended remain/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons as explained in the prior office action and for the reasons as explained below.

The claimed method as amended remains indefinite with regard to the claimed phrase such as “**temporal**” separation of oxygen evolution as explained in the prior office action because it is uncertain as claimed when oxygen “separation” occurs in the claimed method. It is unclear as claimed from what gas the “oxygen evolution” is separated in the claimed method and what gas is generated or collected in the claimed method. The claimed method appears to be

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drawn to a generation of hydrogen but the resulting gas is a gas mixture comprising hydrogen as claimed, for example: see the final step (f) of claim 1. The algal culture produces both oxygen and carbon dioxide at the same time in the claimed method, for example: see the step (e) of claim 1. Thus, the concept of “temporal” separation is unclear in the claimed method. It is uncertain what is a final gas product. It is uncertain whether and/or when separation of different gases occurs in the claimed method. Is it a complete “separation” in time? What are time periods?

The claimed method as amended remains indefinite with regard to step of “depleting a nutrient”. It is unclear whether the nutrient was present in a medium of step (a), whether the nutrient is used (depleted or reduced) during microbial grow to a concentration less than 0.5 millimolar (see claim 3) or whether the medium is replaced by another medium without the claimed nutrient(s). It is uncertain as claimed whether a depleting step is an active step such as changing one nutrient medium for another medium or whether a depleting step is an inherent process as the result of growing microorganisms and, thus, using/depleting/reducing available nutrients in the medium. It appears from the as-filed specification that the culture has been deprived from sulfur by replacing the first culture medium with the second sulfur-free medium (page 5, last 3 lines and/or page 8, last par.). Yet, the claimed invention does not appear to point out the active step of depriving or removing selected nutrient as intended and/or argued by applicants, for example: see response page 4, last paragraph. In addition, it is uncertain as claimed whether one nutrient, two nutrients or all 3 nutrients (sulfur, iron and manganese) are

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depleted from the medium, for example: see phrase “and/or” in step (b) of claim 1. Thus, the claimed Markush group is improper as claimed.

Claim 1 as amended remains indefinite and confusing with regard to the use of light energy during the whole process because it is not particularly clear whether or not some differences are intended between “illuminated conditions” in step (a) and “light” condition in the instant step (e). It is also uncertain whether “the light of saturating yellow actinic excitation”, which is applied to the sample in step (d), is also intended for the whole process including steps (a), (b) and (e).

Claim 1 as amended remains indefinite with regard to the phrase “controlling” because it is unclear what is done or what protocol is applied in this step (e) in order to control rates of oxygen production and of respiration as intended. The claimed method encompasses some measurements in the samples drawn from the whole culture but it is unclear whether and how the results of steps (c) and (d) have been evaluated to control events of the step (e) as claimed. It is uncertain what are the active steps which lead to “controlling” the equal rates of gas production as claimed. In addition, there is some confusion as claimed with respect to the antecedent basis for “a rate” of cellular respiration in the step (e) since there some other rate of cellular respiration in step (c) as claimed.

Claim 2 as amended remains indefinite because is not particularly clear whether hydrogen is generated from both water and from “endogenous substrate”. Please, provide clarification and insert “from” second time is that is intended.

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Claim 5 remains indefinite with respect to the limitation “a plurality of cycles”. The pending claim 5 appears to refer to the method of the original claim 1 but not to the presently amended claim 1 and, thus, the steps recited in the claim 5 lack proper and sufficient antecedent basis in the amended claim 1. For example: the presently amended claim 1 does not contain “collecting” step. Yet, claim 5 refers to some unidentified “collecting” step. Thus, it is uncertain what steps are repeated for a plurality of cycles as required in the method of claim 5.

Claim 5 remains indefinite with respect the phrase “additional substrate”. It is not particularly clear as claimed whether “substrate” of claim 5 is “additional endogenous substrate” for generation of hydrogen. Please, amend claim 5 accordingly to the substrate as intended to provide a proper antecedent basis in the claimed method.

Claim 7 as presently pending appears to refer to the method of the original claim 1 but not to the presently amended claim 1 and, thus, the active steps recited in the claim 7 lack the proper and sufficient antecedent basis in the presently amended claim 1. For example: the phrase “generating” clearly lacks antecedent basis and it is uncertain whether the step of “incubating” is directed to growing and/or incubating the sample or the whole culture.

Claim 8 remains indefinite with respect to the phrase “substrate”. It is not particularly clear as claimed whether “substrate” of claim 8 is “endogenous substrate” for generation of hydrogen or whether “substrate” of claim 8 might be substrate in a culture medium.

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New matter

Claims 1-3, 5-8 and 10 as amended remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention as explained in the prior office action and for the reasons as explained below.

Insertion of the limitation drawn to “controlling” rates of oxygen production and of cellular respiration in step (e) raises the issue of new matter with respect to the proper support in the as-filed specification.

First, the insertion of this limitation is a new concept because it does not have a literal support in the as-filed specification by way of a generic disclosure of “controlling” as an active step as presently claimed.

Further, the insertion of this limitation appears to encompass the active step of “controlling” rate of oxygen production to be equal or less than respiration in the whole culture after the rate of oxygen production and the rate of respiration are measured in the samples withdrawn from the whole culture system. There are some particular examples in as-filed specification which demonstrate how oxygen production and cellular respiration were measured in some samples (page 6). But there is no specific examples in the as-filed specification which demonstrate how these measurements are evaluated and/or how the results of “measuring” are applied to the whole culture in order to control the rate of oxygen production to be equal or less

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than respiration in the whole culture as required by the presently claimed method. Thus, it appears that there is no written description of “controlling” step as an active step.

This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the newly inserted limitation of “controlling” the rates to be equal or less as claimed raises a question of a new matter because either it is uncertain what is done to provide for “controlling” as claimed or the “controlling” step is lacking support in the written description.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3, 5-8 and 10 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,442,211 [IDS-1] and US 4,010,076 [A] taken with Wykoff et al. [U].

Claims are directed to a process for temporal separation of oxygen evolution and for hydrogen production by photosynthetic algal microorganism wherein the process comprises steps of growing the algal microorganism in a medium under illuminated conditions in order to accumulate endogenous substrate, depleting (reducing) nutrients including sulfur, iron or manganese from the medium, sealing the microorganism from atmospheric oxygen, incubating the sealed microorganism under illuminated conditions and collecting gaseous products including

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hydrogen. Some claims are further drawn to hydrogen generation from water and accumulated substrate under illuminated conditions. Some claims are further drawn to a repetition of process or to a plurality of cycles. Some claims are further drawn to accumulation of endogenous substrates such as acetate or carbohydrate or proteins. Some claims are further drawn to the use of algal culture such as *Chlamydomonas reinhardtii*.

The cited references are relied upon as explained in the prior office action and repeated herein.

US 4,442,211 [IDS-1] discloses a process of a “temporal separation of oxygen evolution” and hydrogen production by a photosynthetic algal microorganism such as *Chlamydomonas reinhardtii* wherein the process comprises steps of growing the microorganism in a medium under illuminated conditions in order to accumulate endogenous substrate and, thus, depleting nutrients including sulfur, iron or manganese from the original medium by growing algal cells and by accumulating endogenous substrates. The cited method also comprises step of sealing the microorganism from atmospheric oxygen and/or incubating the microorganism under illuminated conditions or in the light in the environment free from atmospheric oxygen and carbon dioxide by passing inert gas through the culture system. The cited method comprises step of collecting gaseous products including hydrogen (col. 1 lines 62-65). The disclosed method teaches hydrogen generation by algal culture of *Chlamydomonas reinhardtii* from water and accumulated substrates under illuminated conditions (col. 1, lines 60-68 and col. 2, lines 1-3). The cited patent also encompasses a repetition of the process steps or a plurality of cycles (col. 3, lines 32-45).

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Although, the method of the cited patent US 4,442,211 [IDS-1] is not particularly clear whether sulfur, iron or manganese in the medium were depleted to the concentration of 0.5 millimolar or less as required by the presently claimed method (see claim 3), it is reasonably expected that the growing step results in the substantial depletion or in the substantial reduction of these inorganic nutrients particularly in view that the starting or the original culture medium contains these inorganic compounds as "trace elements" or in amounts less than 0.5 millimolar (col. 2, lines 54-55). Although, the method of the cited patent US 4,442,211 [IDS-1] does not disclose active steps of "measuring" rates of oxygen production and respiration, the whole process occurs under the same conditions including exclusion of atmospheric oxygen, anaerobic conditions, culture illumination, depletion or reduction of selected nutrients and the process of the cited patent results in the production of hydrogen. Thus, the method of the cited patent US 4,442,211 [IDS-1] is substantially similar to the presently claimed method.

The cited patent US 4,010,076 [A] is relied upon for the teaching of a process for hydrogen production by various photosynthetic algal cultures including blue, green and red algal cultures which comprises generating of hydrogen from water in the "spent" microbial cultures or in the culture media which is depleted from nutrients over some period of incubation (table 1). The cited patent discloses a process for generating hydrogen in the absence of atmospheric oxygen under illumined conditions in the "spent" culture with reduced nutrients by utilizing bacterial cells (example 1) as required by the presently claimed method. The cited patent also

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teaches the value of microbial hydrogenase for producing useful products including hydrogen (col. 1, line 17).

Thus, the methods for hydrogen production of the cited patents US 4,442,211 and US 4,010,076 are substantially similar to the presently claimed method.

However, the cited patents US 4,442,211 and US 4,010,076 are silent with regard to the active and/or controlled depletion or removal of selected nutrients including sulfur from the culture medium for controlled induction of a “temporal separation of oxygen evolution” and hydrogen production by algal microorganisms.

But the cited reference by Wykoff et al. [U] demonstrates that decline of oxygen production by photosynthetic microorganisms is induced by nutrient starvation and that the photosynthetic evolution of oxygen in the algal culture of *Chlamydomonas reinhardtii* is induced by sulfur starvation or removal of sulfur from the culture medium (abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the prior art methods of the cited patents US 4,442,211 and US 4,010,076 by introducing an active step directed to controlling the nutrient depletion or sulfur starvation with a reasonable expectation of success in decreasing oxygen production and, thus, avoiding deactivation of hydrogenase in the presence of oxygen for the benefit in hydrogen generation as intended for the presently claimed invention because the prior art teaches that depletion from the culture medium of sulfur results in the decline of photosynthetic rate of oxygen production {Wykoff et al. [U]} and because it is known that

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hydrogen is produced from water under anaerobic illuminated conditions by various photometabolically active algal microorganisms including red, green and blue green algae {US 4,442,211 [IDS-1], US 4,010,076 [A]} by action of hydrogenase {US 4,010,076}. One of skill in the art would have been motivated to separate oxygen and hydrogen production for the expected benefits of maximizing the production of hydrogen with the hydrogenase containing microbial cultures including various algal cultures. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicants' arguments filed 5/15/2003 [Paper No. 15] have been fully considered but they are not all found persuasive for the reasons below.

The main applicants' argument is drawn to the idea of unexpected metabolic switch after removal of sulfur from the algal culture which provides for equal rates of photosynthesis and respiration thereby avoiding deactivation of dehydrogenase (see response page 5). Yet, the claimed method does not clearly indicate how the selected nutrients including sulfur are removed from the growing culture system and/or how the "controlling" step is performed. The prior art method of the cited patent US 4,010,076 encompasses the use of "spent" culture wherein the nutrients including sulfur have been used for microbial growth and, thus, the method comprises a step of depleting nutrients within the scope of the claimed invention. The method for temporal

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separation of oxygen evolution and hydrogen production of the cited US 4,442,211 comprises step of growing algal culture and, thus, using/depleting nutrients including sulfur as required by the claimed invention, wherein the metabolic switch that is argued is an inherent mechanism of action under identical condition. Thus, the innovation as argued (see response page 5) such as a continuous production of hydrogen without deactivation of dehydrogenase after the methabolic switch in the absence of sulfur appears to be a mechanism of action rather than the active step in the claimed method for hydrogen production.

Applicants argue that the cited patent US 4,442,211 (Greenbaum) lacks step of “depleting” sulfur (page 7, last par.). Yet, the step of “depleting” nutrient as claimed does not indicate a structural difference from the step of using/depleting nutrient while growing the culture of microorganisms in the method of US 4,442,211 (Greenbaum).

Applicants appear to argue that the cited patent US 4,442,211 (Greenbaum) lacks or it does not recognize the event of inducing reversible hydrogenase (response page 8, first paragraph). However, this argument is directed to a mechanism of action of the hydrogen production by microbial culture rather than to the structural differences in the method protocols or in the active steps of the methods. Moreover, it is uncertain as claimed and as disclosed by applicants what is actually done in the applicants’ method during “controlling” or “inducing” step. Thus, the prior art method which comprises the similar, if not identical, steps and/or structural elements as the claimed method, is also substantially similar in the final results as

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intended such as “temporal separation of oxygen evolution” and hydrogen production and, thus, it provides for avoiding a deactivation of hydrogenase as intended and/or argued.

With regard to the method of the cited US 4,010,076 (Weetall) applicants’ main argument is directed to the concept of a mechanism of hydrogen production by algal culture rather than to the differences in the protocols of active steps (response page 8, par. 2-3). However, the method of US 4,010,076 (Weetall) comprises the similar, if not the same, steps and structural elements as the claimed method and, thus, it is reasonably expected to include the same mechanism or conditions for hydrogen production or the same “temporal separation of oxygen evolution” and hydrogen production which provides for avoiding a deactivation of hydrogenase as intended and/or argued.

With regard to the cited reference by Wykoff et al. applicants appear to argue that it does not teaches hydrogen production (page 8, last paragraph). However, the cited reference is relied to demonstrate that the active step of removing sulfur leads to the decrease in oxygen production, thus, to avoiding hydrogenase deactivation. Therefore, the cited reference by Wykoff et al. supports the inherent event in the method for hydrogen production of the cited patents US 4,442,211 (Greenbaum) and US 4,010,076 (Weetall).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (response page 9, par. 3), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of

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ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

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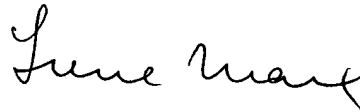
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

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August 4, 2003.



IRENE MARX
PRIMARY EXAMINER